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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/919,504	07/31/2001	R. Martin Emanuele	19720-0625 (42896-261843)	3166

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Jeffery B. Arnold
KILPATRICK STOCKTON LLP
SUITE 2800
1100 Peachtree Street
Atlanta, GA 30309-4530

EXAMINER
SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 01/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/919,504	Emanuele
Examiner	**Art Unit**
Richard Schnizer	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 30, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-38* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☒ The drawing(s) filed on *Mar 5, 2002* is/are a) ☒ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. An amendment was received and entered as Paper No. 8 on 10/30/02. Applicant's election with traverse of group I is acknowledged. After further consideration, the restriction requirement is withdrawn, and claims 1-38 are under consideration in this Office Action.

Priority

2. Applicant has claimed priority under 35 USC 120 to a variety of US patent applications. This priority claim cannot be granted for the following reasons. All instant claims embrace compositions comprising an octablock copolymer and a nucleic acid, however none of the priority documents provides support for this combination of limitations. For this reason, the filing date of the instant claims must be the filing date of the instant application, 7/31/01.

Claims

3. Please note that the application as filed contained two claims numbered 33 and two claims numbered 34. The claims have been renumbered in accordance with 37 CFR 1.126. The second instance of claim 33 is now claim 37, and the second instance of claim 34 is now claim 38.

Claim Objections

4. Claims 6, 14, 24, and 32 are objected to because they are ungrammatical. The article "an" in the phrase "an low molecular weight alcohol" should be replaced with the article "a".

Compliance with Sequence Rules

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s). This application clearly fails to comply with the requirements of 37 C.F.R.1.821-1.825. Applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). **At page 31, line 30 the specification discloses an oligonucleotide that is longer than 10 bases in length but which is not identified by a SEQ ID NO, and Applicant has not provided a Sequence Listing in either a computer readable form or on paper.**

Applicant must provide:

An initial computer readable form (CRF) copy of the "Sequence Listing".

An initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

6. Claims 1-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for therapeutic methods and compositions capable of altering nucleic acid function, as disclosed in the prior art, wherein the therapy does not rely on the use of one or more nucleic acids to alter the function of another nucleic acid, does not reasonably provide enablement for therapeutic compositions and methods that rely one the use of nucleic acids to alter the function of other nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Nature of the Invention

7. Claims 1-18, 20-22, 28-30, and 34-36 are drawn to therapeutic compositions for treating animals. The compositions must comprise a compound capable of altering nucleic acid function, and an octablock copolymer. Claims 19, 23-27, 31-33, 37, and 38 are drawn to methods of delivering to animals compounds capable of altering nucleic acid function, and an octablock copolymer. The specification discloses no purpose for this method other than therapy or immunization.

Breadth of the Claims

8. The claims are not limited in terms of the diseases or disorders which can be treated. All claims embrace the use of nucleic acids as the compounds which can alter nucleic acid function. In other words, the claims embody methods of delivering nucleic acids, i.e. genes, oligonucleotides, antisense oligonucleotides, triplex DNA compounds, or ribozymes, for the purpose of therapeutically altering nucleic acid function in vivo. The specification also teaches that the claimed compositions and methods can be used for genetic immunization. The claims do not limit the animal which can be immunized, or the diseases against which immunization is therapeutic.

Background

9. Prior to the time of the invention it was well known in the art that octablock copolymers with the characteristics required by the instant claims could be used to deliver non-nucleic acid therapeutic molecules in vivo. See rejections under 35 USC 102 and 103 below. For example, Jansen et al (US Patent 4,902, 500, 2/20/1990) taught that Pluronics T1501, T1301, T1101,

T150R1, T130R2, and T110R1, could be used to deliver antibodies in vivo for therapeutic purposes (see column 1, lines 33-37, column 2, lines 7-17, and column 2, line 63 to column 3, line 9. As noted below under 35 USC 103 rejections, the use of octablock copolymers to deliver in vivo therapeutic compositions that happen to comprise nucleic acids, wherein the nucleic acids are not required for therapy, was also enabled at the time of the invention. The state and unpredictability of the art of therapeutic use of nucleic acids in vivo at the time of the invention is discussed below.

State of the Art and *Predictability of the Art*

10. At the time the invention was made, successful implementation of gene therapy protocols was not routinely obtainable by those skilled in the art. This is reflected by two recently published reviews. Verma et al (Nature 389: 239-242, 1997) teach that "there is still no single outcome that we can point to as a success story (p. 239, col 1). The authors state further, "Thus far, the problem has been the inability to deliver genes efficiently and to obtain sustained expression" (p.239, col. 3). Anderson (Nature 392:25-30, 1998) confirms the unpredictable state of the art, stating that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human disease" (p. 25, col. 1) and concluding, "Several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered" (p.30). More recently, Romano et al (2000) reviewed the general state of gene therapy, and found that the problems relating to gene delivery and expression discussed above persisted. See entire document, especially, last sentence of abstract; last sentence of

column 1 on page 20 to column 2, line 6; page 21, column 1, lines 1-9 and 18-21; sentence bridging columns 1 and 2 on page 21; and first sentence of last paragraph on page 21. This idea was echoed by Somia and Verma (2000), who noted that delivery vehicles still represented the Achilles heel of gene therapy, and that no single vector existed that had all of the attributes of an ideal gene therapy vector. See page 91, column 1, lines 5-13 of first paragraph.

11. The state of the art with respect to antisense therapies is set forth by Crook (In Basic Principles of Antisense Therapeutics, Springer-Verlag, Eds, New York, pgs. 1 and 4), who teaches that although antisense techniques have progressed rapidly, "the technology remains in its infancy", and the utility of the approach is still debatable (pg. 1, Introduction). Crook points out several factors which may influence the biological effect of an antisense oligonucleotide (AODN), including the rate of uptake of the AODN, rate of distribution within the target cell, stability within the target cell, local concentration of the oligonucleotide, and the concentration and stability of the target mRNA (pgs. 1 and 4). Furthermore, Branch (Trends in Biochem Sci 23: 45-50, 1998) teaches that selection of appropriate antisense sequences is difficult because secondary structures of mRNAs *in vivo* frequently restrict access of antisense oligonucleotides to the target sequence (page 45, col. 3. first para., page 48, last para. and page 49). Branch states, "Since accessibility cannot be predicted, rational design of antisense molecules is not possible" (page 49, col. 2, last para.).

12. The state of the art of genetic immunization was set forth by McCluskie et al (Molecular Medicine 5(5): 287-300, 1999). McCluskie considers the effects of the routes of administration of

DNA vaccines on the quality of any resulting immune response, and considers the relevance of animal models to practice in humans. Pertinent to the instant case, McCluskie teaches that "promising results in animal models have not been realized in human trials and considerable effort is now being focused at understanding this difference and developing ways of improving the efficacy of DNA vaccines." See final sentence of first paragraph on page 288, column 1. McCluskie points out that "[t]he strength and nature of immune responses in mice with DNA vaccines appear to be influenced by a number of factors [citation omitted]; however, these variables may not be of similar importance in larger animals including humans. As such, optimization methods developed in mice may not necessarily be applicable to humans." See page 288, column 2, first full paragraph. In fact, it is clear that some vaccines developed in mice do not function at all in some primates. At page 296, column 2, second full paragraph, McCluskie states that "[t]he realization that results in mice often do not predict the situation in humans also led to a large number of DNA vaccine studies in non-human primates, including Aotus monkeys, rhesus monkeys, and chimpanzees. IM injection of plasmid DNA vaccines, while highly immunogenic in mice was found to be only relatively so in chimpanzees and essentially not at all in Aotus monkeys. Furthermore, although early human studies have demonstrated the safety and potential of DNA vaccines, results obtained have not been as good as predicted from animal models. Collectively, these results indicate that no animal model may be ideal for prediction of efficacy in humans [citations omitted]."

13. McCluskie concludes "[i]n summary, mice may have limited value for choosing the best route of DNA vaccine delivery for humans. While efficacy in murine models has preceded the successful development of many human vaccines, it is probably safe to say that any vaccines that work in a human will work in a mouse, but not necessarily *vice versa*. Therefore it is difficult to predict from mouse studies the potential of a new vaccine in humans. In fact, in those human trials that have been carried out, none of the DNA vaccines induced the strong immune responses that had been seen in mice with the same vectors. Furthermore, although non-human primate models are frequently used for development and testing of human vaccines, it is not clear how predictive they will be in the case of DNA vaccines where efficacy, by virtue of the requirement to first transfect cells and express antigens, relies on many factors other than immunological responses to the antigen. We will not know the answer to this until after greater experience has been achieved in non-human primates and human clinical trials." See paragraph bridging pages 296 and 297.

Level of Skill of Those in the Art.

14. From the foregoing it is clear that gene therapy, antisense therapy, and genetic immunization in humans were highly unpredictable at the time the invention was filed, and even those of the highest level of skill in the biotechnological art could not perform these methods with routine success.

Guidance and Examples in the Specification

15. The specification teaches no working examples of gene or antisense therapy. A single example of the induction of an immune response in a mouse by administration of a block copolymer and a nucleic acid encoding a viral antigen is given at page 34, lines 18-30. However, the specification fails to disclose the nature of the copolymer used in the procedure, so it is not clear that the copolymer was an octablock copolymer of the instant invention, rather than a linear copolymer. Further, there is was no apparent protective or therapeutic effect disclosed. The specification provides no guidance for improving the state of the art of in vivo gene expression, oligonucleotide design, or genetic immunization such that one of skill in the art could overcome the art-recognized unpredictability in these methods as summarized above.

Amount of Experimentation Required to Practice the Invention

16. In view of the state of the art of nucleic acid mediated therapies, including genetic immunization, the unpredictability associated with these methods, the failure of those of skill in the art to routinely obtain success in these methods, and the failure of the specification to address the art-recognized difficulties associated with these methods, one of skill in the art would have to perform undue experimentation in order to practice the invention commensurate in scope with the claims.

Written Description

17. Claims 1-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

18. Claims 1-38 are drawn to the genus of compounds "capable of altering nucleic acid function". As discussed above under enablement, it is clear from the specification that these compounds should be therapeutic in nature, so the claimed genus is considered to be compounds capable of altering nucleic acid function to therapeutic effect in an animal. The breadth of the claimed genus appears to be vast. At page 29, lines 32-35 Applicant implies that the claimed genus embraces **any and all** compounds that can alter nucleic acid function, and is not limited to only oligo- or polynucleotides. However, in view of the limitation of claims 5, 13, 23, and 31 to the subgenuses of genes, oligonucleotides, antisense, triplex compounds, and ribozymes, the written description analysis will begin with a consideration of these subgenuses.

19. In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species has been described by complete structure, such as nucleotide sequence, next it is determined whether a representative number of species has been described by other relevant identifying characteristic. Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov).

20. At page 31, line 30, Applicant discloses by complete structure an antisense oligonucleotide corresponding to regions of the *art/trs* genes of HIV. However it is unclear as to whether this oligonucleotide can be used to therapeutic effect because the specification discloses no working

example, and because the art of oligonucleotide mediated therapy is highly unpredictable as established above under enablement. So, it is unclear whether or not this oligonucleotide is a member of the claimed genus. The specification discloses by complete structure no other oligo- or polynucleotide that can be used for therapy. The specification discloses by relevant identifying characteristic, i.e. by name, two other genes purported to be useful in therapy. The specification discloses the ADA gene and the herpes simplex virus gD gene at page 32, lines 30-33 and page 33, line 26-28, respectively. No other oligo-or polynucleotides are disclosed by any relevant identifying characteristic. There is no evidence of record that either of these genes can be used to therapeutic effect.

21. The question now arises as to whether or not this disclosure constitutes a description of a representative number of species. The Guidelines on Written Description indicate that what constitutes a representative number of species varies inversely with the skill and knowledge in the art, and that in an unpredictable art such as gene therapy, adequate written description of a genus cannot be achieved by disclosing only one species within the genus. In this case, it is not clear that the specification has disclosed any single species that is representative of any of one the subgenuses set forth in claims 5, 13, 23, and 31, therefore one of skill in the art could not conclude that applicant was in possession of the claimed invention at the time of filing.

22. In consideration of the broader claims embracing any and all compounds that alter gene function, clearly the specification fails to satisfy the written description requirement because it fails to adequately describe the subgenuses set forth in claims 5, 13, 23, and 31. Furthermore,

while the specification discloses a list of antibiotics and antivirals at page 14, lines 20-33, this cannot serve as an adequate description of the subgenus comprising non-nucleic acid compounds, because this subgenus includes drugs that are totally unrelated to antibiotics and antivirals such as cytokines, immunosuppressants, hormones, growth factors, and any other drug that has any effect, direct, or indirect, on gene expression. The specification does not describe such compounds by reduction to practice, complete structure, relevant identifying characteristics, or by any other means set forth in the Written Description Guidelines. For these reasons one of skill in the art could not conclude that Applicant was in possession of the claimed invention at the time of filing.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

23. Claims 1-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

24. Claims 1-38 are indefinite because they recite "human" and "animal" as alternatives. This is confusing because humans are animals. Deletion of the word "human" is suggested.

25. These claims also recite "the compound" without proper antecedent basis. For example, claim 1 lines 18 and 19 recite "about 40% of the compound by weight", in apparent reference to the POE portion of the copolymer. Similarly lines 22 and 23 of claim 1 recite "about 90% of the

compound by weight". These passages appear to refer to the octablock copolymer, but the only antecedent for "the compound" is "a compound capable of altering nucleic acid function admixed with a block copolymer" in lines 5 and 6.

26. Claims 5, 13, 23, and 31 are indefinite because the metes and bounds of the word "genes" are unclear. The specification fails to define the term, and there is no single art-recognized definition. For example, the term is regularly used to refer only to a coding sequence (open reading frame), but is also regularly used to refer to a genetic unit comprising 5' and 3' noncoding sequences, and introns as well. It is unclear which definition Applicant intends, so it is unclear what are the metes and bounds of the claims.

27. Claims 7, 15, 25, and 37 are indefinite because they contain the trademark/trade name "Tween 80". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material of product, the claim does not comply with the requirements of 35 USC 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be properly used to identify any particular material or product. A trademark or trade name is used to identify a source of goods, not the goods themselves. Thus a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case the trademark or trade name is used to identify or describe polyoxyethylene sorbitan monooleate and, accordingly, the identification or description is indefinite. See MPEP 2173.05(u).

28. Claims 24, 25, 32, and 37 are confusing because the purpose in the method of further including a surfactant and an alcohol is unclear. The claims fail to recite at what step the surfactant and alcohol should be added, or to what composition they should be added. Claims 7 and 15 are indefinite because they contain the trademark/trade name "Tween 80". Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material of product, the claim does not comply with the requirements of 35 USC 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be properly used to identify any particular material or product. A trademark or trade name is used to identify a source of goods, not the goods themselves. Thus a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case the trademark or trade name is used to identify or describe polyoxyethylene sorbitan monooleate and, accordingly, the identification or description is indefinite. See MPEP 2173.05(u).

Claims 26 and 38 are confusing because the purpose in the method of further including an expression vector is unclear. The claims fail to recite at what step the expression vector should be added, or to what composition it should be added.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

29. Claims 1-4, 9-12, 17-22, 27-30, and 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Hunter et al (US Patent Nos. 5,234, 683, issued 8/10/93).

No amdt on 13

30. It is noted that the publication date of Hunter is later than the claimed priority date of the instant Application. However, for the reasons stated above under "Priority", the priority date of the instant claims is considered to be 7/31/01, and a rejection under 102(b) is proper.

31. Hunter teaches methods of stimulating an immune response in an animal by administering to the animal an octablock copolymer (see claims 1-12). The copolymers may be administered in a composition comprising an antigen (see abstract). The process of stimulating an immune response necessarily involves stimulating gene expression, thereby meeting the claim limitation of "altering nucleic acid function".

32. The limitations of the copolymers recited in instant claims 1-4, 17-22, and 27-30 are met in at least claim 1 of Hunter which recites an octablock copolymer in which the POP portion is approximately 6750 D. It is noted that instant claims 3 and 4 require POP portions of

approximately 5750 and 5220 Daltons, respectively. However, the specification fails to define the metes and bounds of "approximately" in this context, so it has been given its broadest reasonable interpretation. It is considered that "approximately 6750 D" embraces both 5750 and 5220 Daltons. In any event, claim 4 of Hunter teaches an octablock copolymer in which the POP portion is approximately 5750 D, clearly anticipating instant claim 3.

33. The limitations of the copolymers recited in instant claims 9-12 and 33-36 are met in at least claim 11 of Hunter which recites a reverse octablock copolymer in which the POP portion is approximately 6750 D. It is noted that instant claims 11 and 12 require POP portions of approximately 5750 and 5220 Daltons, respectively. However, as above, it is considered that "approximately 6750 D" embraces both 5750 and 5220 Daltons. In any event, claim 12 of Hunter teaches a reverse octablock copolymer in which the POP portion is approximately 5750 D, clearly anticipating instant claim 3.

Thus Hunter anticipates the claims.

Claims 1-4, 9-12, 17-22, 27-30, and 33-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Jansen et al (US Patent 4,902,500, issued 2/20/90).

No nucleic acids

34. Jansen teaches methods of stabilizing antibodies in octablock copolymers, and administering the antibodies to animals. For example, Jansen taught that Pluronics T1501, T1301, T1101, T150R1, T130R2, and T110R1, could be used to deliver antibodies in vivo for therapeutic purposes (see column 1, lines 33-37, column 2, lines 7-17, and column 2, line 63 to

column 3, line 9. Pluronic T1501 corresponds to the octablock copolymer recited in instant claims 1, 2, and 17-20. Pluronic T1301 corresponds to the copolymer in instant claims 3 and 21. Pluronic T1101 corresponds to the copolymer in instant claims 4 and 22. Pluronic T150R1 corresponds to the copolymer in instant claims 9, 10, 27, 28, 33, and 34. Pluronic T130R1 corresponds to the copolymer in instant claims 11, 29, and 35. Pluronic T110R1 corresponds to the copolymer in instant claims 12, 30, and 36.

Thus Jansen anticipates the claims.

35. Claims 1-5, 8-13, 16-23, 26-31, 33-36, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Lemieux et al (US Patent 6,359,054, issued 3/19/02).

36. Lemieux teaches methods of delivering to a patient a composition comprising octablock block copolymers and nucleic acids, (see e.g. claim 13 at column 49). The nucleic acid can be an expression vector, antisense, ribozyme, or oligonucleotide (see column 21, lines 15-29). The octablock copolymers useful in the invention include a variety of conventional and reverse orientation octablock copolymers set forth at column 15, lines 8-45 and 25-31, including Pluronics T1101, T1301, T1501 and T110R1, T130R1, and T150R1 (see column 14, lines 34-36 and 54-62). Pluronic T1501 corresponds to the octablock copolymer recited in instant claims 1, 2, and 17-20. Pluronic T1301 corresponds to the copolymer in instant claims 3 and 21. Pluronic T1101 corresponds to the copolymer in instant claims 4 and 22. Pluronic T150R1 corresponds to the copolymer in instant claims 9, 10, 27, 28, 33, and 34. Pluronic T130R1

corresponds to the copolymer in instant claims 11, 29, and 35. Pluronic T110R1 corresponds to the copolymer in instant claims 12, 30, and 36.

Thus Lemieux anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

37. Claims 6, 7, 14, 15, 24, 25, 32, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunter et al (US Patent 5,234,683).

38. Hunter teaches methods of stimulating an immune response in an animal by administering to the animal an octablock copolymer (see claims 1-12). The limitations of the copolymers recited in instant claims 6, 7, 24, and 25) are met in at least claim 1 of '683. The limitations of the copolymers recited in instant claims 14, 15, 24, 25, 32, and 37 are met in at least claim 11 of '683 which recites a reverse octablock copolymer. Hunter teaches compositions for administration to animals that comprise block copolymers in the concentration of 0.5-5% (see e.g. column 24, lines 20-29). The block copolymers are considered to be surfactants (see column 17, lines 9-17), Thus Hunter teaches a composition comprising 0.5-5% by weight of a surfactant. Hunter also teaches

that the block copolymers may be solubilized in ethanol (see column 2, lines 36-38). It is noted that claims 1-4, 9-12, 17-22, 27-30, and 33-36 are anticipated by Hunter (see 35 USC 102 rejections above).

39. Hunter does not teach a composition comprising both 0.5-5% by weight of a surfactant and 0.5- 5% by volume of a low molecular weight alcohol.

40. It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the compost of Hunter to comprise both 0.5-5% by weight of a surfactant and 0.5- 5% by volume of ethanol. One would have been motivated to do so because Hunter teaches that 0.5-5% by weight of a block copolymer is an appropriate concentration for administration, and because Hunter teaches that copolymers may be dissolved in ethanol prior to dilution in cold aqueous solution (see column 2, lines 36-38). The concentration of ethanol in the composition must be considered to be a result effective variable that is obvious to optimize. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating that this concentration is critical. See MPEP 2144.05(b). Hunter teaches the general conditions of the claims, i.e. a composition comprising the appropriate amount of a surfactant as well as ethanol. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Thus the invention as a whole was prima facie obvious.

41. Claims 1, 2, 5, 8, 17-20, 23, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pahlson et al (Acta Pathol. Microl. Immunol. Scand. B (1986) 94(3): 117-125), in view of Woodard (Laboratory Animal Science (1989 May) 39(3): 222-225).

42. Pahlson teaches a method of inducing an immune response in a mouse by administering whole bacteria emulsified in Freund's complete adjuvant. See abstract. Whole bacteria are considered to comprise expression vectors (chromosomes) comprising sequences (promoters) that can alter the function of nucleic acids (coding sequences). Further, whole bacteria would also be considered to comprise ribozymes as part of their ribosomes, as well as antisense oligonucleotides (Okazaki fragments).

43. Pahlson does not teach an octablock copolymer.

44. Woodard teaches that the octablock copolymer T1501 is equivalent to Freund's complete adjuvant for the purpose of stimulating antibody production. See abstract.

45. It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the T1501 octablock copolymer of Woodard for the Freund's complete adjuvant of Pahlson. One would have been motivated to do so because Woodard teaches that T1501 and Freund's complete adjuvant are equivalent in the art of stimulating antibody production. Regarding the obviousness of art-recognized equivalents, MPEP 2144.06 states in part:

> In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents... Smith v. Hayashi, 209 USPQ 754 (Bd. of Pat. Inter. 1980) (The mere fact that phthalocyanine and selenium function as equivalent photoconductors in the claimed environment was not sufficient to establish that one would have been obvious over the other. However, there was evidence that both phthalocyanine and selenium were known photoconductors in the art of

> electrophotography. "This, in our view, presents strong evidence of obviousness in substituting one for the other in an electrophotographic environment as a photoconductor." 209 USPQ at 759.).
>
> **An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious.** In re Fout, 675 F.2d 297, 213 USPQ 532 (CCPA 1982).

Emphasis added. Because T1501 and Freund's complete adjuvant are art-recognized equivalents in stimulating antibody production, it would have been obvious to substitute one for the other, even in the absence of an express suggestion to do so.

Therefore the invention as a whole was *prima facie* obvious.

46. Claims 3, 4, 9-13, 16, 21, 22, 27-31, 33, 35, 36, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pahlson et al (Acta Pathol. Microl. Immunol. Scand. B (1986) 94(3): 117-125) and Woodard (Laboratory Animal Science (1989 May) 39(3): 222-225), as applied to claims 1, 2, 5, 8, 17-20, 23, and 26 above, and further in view of Jansen et al (US Patent 4,902,500, issued 2/20/90).

47. The teachings of Pahlson and Woodard are summarized above, and can be combined to render obvious compositions comprising an octablock copolymer of instant claims 1, 2, 5, 8, 17-20, 23, and 26, and nucleic acids such as expression constructs, ribozymes, and antisense oligonucleotides.

48. Pahlson and Woodard do not teach the octablock copolymers of instant claims 3, 4, 9-13, 16, 21, 22, 27-31, 33, 35, 36, and 38.

Jansen teaches the following octablock copolymers:

Pluronic T1301, corresponding to the copolymer in instant claims 3 and 21.

Pluronic T1101 corresponding to the copolymer in instant claims 4 and 22.

Pluronic T150R1 corresponding to the copolymer in instant claims 9, 10, 13, 16, 27, 28, 31, 33, and 38.

Pluronic T130R1 corresponding to the copolymer in instant claims 11, 29, and 35.

Pluronic T110R1 corresponding to the copolymer in instant claims 12, 30, and 36.

49. It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the T1501 octablock copolymer of Woodard for the Freund's complete adjuvant of Pahlson. One would have been motivated to do so because Woodard teaches that T1501 and Freund's complete adjuvant are equivalent in the art of stimulating antibody production.

50. It would also have been obvious to substitute the T1301, T1101, T150R1, T130R2, and T110R1 of Jansen for Freund's complete adjuvant in the invention of Pahlson. One would have been motivated to do so because these compounds have very close structural similarities to T1501, which is an art recognized functional equivalent of Freund's complete adjuvant, and would reasonably be expected to have similar performance characteristics. See MPEP 2144.09 which reads in part:

> A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (discussed in more detail below) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991)(discussed below and in MPEP § 2144) for an extensive review of the case law pertaining to obviousness based on close structural similarity of chemical compounds.
> See also MPEP § 2144.08, paragraph II.A.4.(c).

Compounds differing regularly by the successive addition of similar groups such as POP or POE monomers are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties.

Therefore the invention as a whole was *prima facie* obvious.

51. Claims 1-5, 8-13, 16-18, 20-22, 28-30, and 34-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kabanov et al (US Patent 5,656,611, issued 8/12/97).

52. Kabanov teaches compositions comprising polynucleotides and octablock copolymers. See abstract and column 7, line 23 to column 8, line 11, especially column 7, lines 40-47). The polynucleotides may be antisense, oligonucleotides, ribozymes, or expression vectors (see column 10, lines 9-28. The copolymers may be of standard or reversed orientation (see column 7, line 64 to column 8, line 3). The compositions of the copolymers, with respect to the amounts and proportions of POE and POP, embrace a wide variety of compounds (see e.g. column 7, lines 48-51 which disclose that POP and POE monomers may be present in each of the four octablock copolymers in amounts of from about 5 to about 400 monomers).

53. Kabanov does not teach the precise limitations of the claims with respect to the molecular weight of the POP portion of the copolymer, or the relative amounts of POP and POE in the copolymers. However, it would have been obvious to one of ordinary skill in the art at the time of the invention to arrive at the compositions set forth in the claims in the process of optimizing the invention of Kabanov for the disclosed purpose of delivering nucleic acids to cells. Because the

Kabanov teaches a range of compositions which overlaps or embraces those of the instant invention, Kabanov teaches the general conditions of the claims. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Thus the invention as a whole was *prima facie* obvious.

Summary

Claims 1-38 are rejected under 35 USC 112, first paragraph, as lacking enablement and written description.

Claims 1-38 are rejected under 35 USC 112, second paragraph as indefinite.

Claims 1-5, 8-13, 16-23, 26-31, 33-36, and 38 are rejected under 35 USC 102 as anticipated.

Claims 5-8, 13-16, 23-26, 31, 32, 37, and 38 are rejected under 35 USC 103 as obvious.

No claims are free of the prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014. Additionally correspondence can be transmitted to the following RIGHTFAX numbers: 703-872-9306 for correspondence before final rejection, and 703-872-9307 for correspondence after final rejection.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.

JEFFREY SIEW
PRIMARY EXAMINER
1/13/03